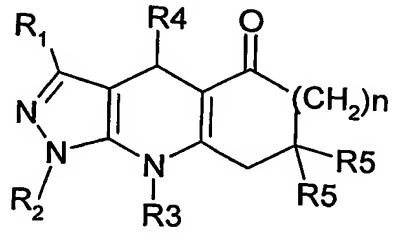
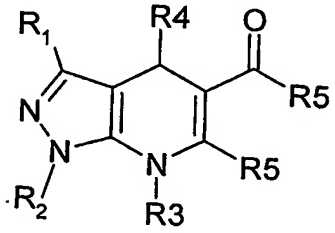
CLAIMS

We claim:

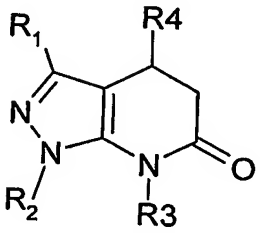
1. A compound having a general structure represented by Formula I, Formula II, or Formula III;



Formula I



Formula II



Formula III

wherein n is an integer selected from 0 to 2;

R_1 and R_2 are each independently a member selected from the group consisting of hydrogen, alkyl, alkenyl, aryl, hetaryl, aralkyl, hetaralkyl, alkyl substituted with at least one substituent, aryl substituted with at least one substituent, hetaryl substituted with at least one substituent, aralkyl substituted with at least one substituent, and hetaralkyl substituted with at least one subsituent;

R_3 is a member selected from the group consisting of hydrogen, alkyl, alkenyl, aralkyl, alkyl substituted with at least one substituent, aralkyl substituted with at least one substituent, $CO\text{-}R_5$, $SO_2\text{-}R_5$; $CO\text{-}O\text{-}R_5$, $CO\text{-}N\text{-}R_4$, and R_5; and

R_4 and R_5 are each independently a member selected from the group consisting of hydrogen, alkyl, alkenyl, cycloalkyl, aralkyl, aryl, alkyl substituted with at least one substituent, cycloalkyl substituted with at least one substituent, aryl substituted with at least one substituent, and aralkyl substituted with at least one substituent.

2. A compound according to Claim 1, with reference to $R_{1\text{-}5}$, whenever the following are used;

alkyl is a straight or branched chain $C_{1\text{-}15}$ alkyl;

cycloalkyl is a $C_{3\text{-}8}$ cycloalkyl;

alkenyl is a straight or branched chain $C_{2\text{-}18}$ alkenyl;

aralkyl is a carbomonocyclic aromatic or carbobicyclic aromatic substituted with a straight or branched chain $C_{1\text{-}15}$ alkyl; and

substituent is selected from the group consisting of nitro, hydroxy, cyano, carbamoyl, mono- or di-C_{1-4} alkyl-carbamoyl, carboxy, C_{1-4} alkoxy-carbonyl, sulfo, halogen, C_{1-4} alkoxy, phenoxy, halophenoxy, C_{1-4} alkylthio, mercapto, phenylthio, pyridylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, amino, C_{1-3} alkanoylamino, mono- or di-C_{1-4} alkylamino, 4- to 6-membered cyclic amino, C_{1-3} alkanoyl, benzoyl, and 5 to 10 membered heterocyclic.

3. A compound according to claim 1, with reference to R_{1-5}, whenever the following are used;

aryl is a carbomonocyclic aromatic or carbobicyclic aromatic;

hetaryl is a heteromonocyclic aromatic or heterobicyclic aromatic containing 1 to 6 hetero-atoms selected from oxygen, sulfur and nitrogen;

aralkyl is a carbomonocyclic aromatic or carbobicyclic aromatic substituted with a straight or branched chain C_{1-15} alkyl; and

substituent is a member selected from the group consisting of halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{1-4} alkoxy, C_{1-4} alkylthio, hydroxy, carboxy, cyano, nitro, amino, mono- or di-C_{1-4} alkylamino, formyl, mercapto, C_{1-4} alkyl-carbonyl, C_{1-4} alkoxy-carbonyl, sulfo, C_{1-4} alkylsulfonyl, carbamoyl, mono- or di-C_{1-4} alkyl-carbamoyl, oxo, and thioxo.

4. A compound according to claim 1, wherein n is 1;

R_1 and R_2 are each independently a member selected from the group consisting of hydrogen, straight or branched chain C_{1-6} alkyl, phenyl, naphthyl, hetaryl, C_{1-6} alkyl substituted with at least one substituent, straight or branched chain C_{1-6} alkylphenyl, phenyl substituted with at least one substituent, benzyl, and benzyl substituted with at least one substituent;

R_3 is a member selected from the group consisting of hydrogen, C_{1-6} alkyl, aralkyl, C_{1-6} alkyl substituted with at least one substituent, CO-R_5, or SO_2-R_5; CO-O-R_5, CO-N-R_4, and R_5;

R_4 and R_5 are each independently a member selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} alkyl substituted with at least one substituent, cycloalkyl, phenyl, and phenyl substituted with at least one substituent, aralkyl, benzyl, and benzyl substituted with at least one substituent; and

substituent is a member selected from the group consisting of halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{1-4} alkoxy, C_{1-4} alkylthio, phenoxyl, halophenoxy, phenylthio, pyridylthio, hydroxy, carboxy, cyano, nitro, amino, C_{1-3} alkanoylamino, mono- or di-C_{1-4} alkylamino, 4- to 6-membered cyclic amino, formyl, mercapto, C_{1-4} alkyl-carbonyl, C_{1-4} alkoxy-carbonyl, sulfo, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-3} alkanoyl, benzoyl, mono- or di-C_{1-4} alkyl-carbamoyl, oxo, thioxo, and 5 to 10 membered heterocyclic.

5. A compound according to claim 1, wherein n is 1, and with reference to R_{1-5}, whenever the following are used;

alkyl is a straight or branched chain C_{1-15};

alkenyl is a straight or branched chain C_{2-18};

aryl is a carbomonocyclic aromatic or carbobicyclic aromatic;

cycloalkyl is a C_{3-8} alkyl ring,

hetaryl is a heteromonocyclic aromatic or heterobicyclic aromatic containing 1 to 6 hetero-atoms selected from the group consisting of oxygen, sulfur and nitrogen;

aralkyl is a carbomonocyclic aromatic or carbobicyclic aromatic and substituted with a straight or branched chain C_{1-15} alkyl;

hetaralkyl is a heteromonocyclic aromatic or heterobicyclic aromatic containing 1 to 6 hetero-atoms selected from the group consisting of oxygen, sulfur, and nitrogen and substituted with a straight or branched chain C_{1-15} alkyl; and

substituent is a member selected from the group consisting of halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} haloalkoxy, C_{1-4} alkoxy, C_{1-4} alkylthio, phenoxyl, halophenoxy, phenylthio, pyridylthio, hydroxy, carboxy, cyano, nitro, amino, C_{1-3} alkanoylamino, mono- or di-C_{1-4} alkylamino, 4- to 6-membered cyclic amino, formyl, mercapto, C_{1-4} alkyl-carbonyl, C_{1-4} alkoxy-carbonyl, sulfo, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, C_{1-3} alkanoyl, benzoyl, mono- or di-C_{1-4} alkyl-carbamoyl, oxo, thioxo, and 5 to 10 membered heterocyclic.

6. A compound according to claim 1, wherein n is 1;

R_1 and R_2 are each independently a member selected from the group consisting of straight or branched chain C_{1-6} alkyl, phenyl, benzyl, naphthyl, straight or branched chain

C_{1-6} alkyl substituted with at least one substituent, phenyl substituted with at least one subsitutent, and benzyl substituted with at least one substituent;

R_3 is a member selected from hydrogen, straight or branched chain C_{1-6} alkyl, C_{1-6} aralkyl, C_{1-6} alkyl substituted with at least one substituent;

R_4 and R_5 are each independently a member selected from the group consisting of hydrogen, straight or branched chain C_{1-6} alkyl, straight or branched chain C_{1-6} alkyl substituted with at least one substituent, cycloalkyl, phenyl, phenyl substituted with at least one substituent, benzyl, and benzyl substituted with at least one substituent; and

substituent is a member selected from the group consisting of methyl, halogen, halophenyloxy, methoxy, ethyloxy phenoxy, benzyloxy, trifluromethyl, t-butyl, and nitro.

7. A compound according to claim 1, wherein n is 1;

R_1 is a member selected from the group consisting of straight or branched chain C_{1-6} alkyl, and phenyl;

R_2 is a member selected from the group consisting of phenyl, C_{1-6} alkylphenyl, C_{1-6} dialkylphenyl, C_{1-6} alkoxyphenyl, halophenyl, dihalophenyl, and nitrophenyl;

R_3 is a member selected from hydrogen and straight or branched chain C_{1-6} alkyl;

R_4 is phenyl substituted with at least one substituent selected from the group consisting of halogen, phenoxy, benzyloxy, halophenoxy, straight or branched chain C_{1-6} alkyl, C_{1-6} alkoxy, and halo-C_{1-4} alkyl and;

R5 is a straight or branched chain C_{1-6} alkyl.

8. The compound of claim 1, wherein n is 1;

R_1 is phenyl or t-butyl;

R_2 is a member selected from the group consisting of methylphenyl, dimethylphenyl, t-butyl, methoxyphenyl, chlorophenyl, dichlorophenyl, fluorophenyl, and nitrophenyl;

R_3 is hydrogen;

R_4 is a phenyl substituted with at least one substituent selected from the group consisting of chlorine, fluorine, phenoxy, benzyloxy, chlorophenoxy, methoxy, ethoxy, and trifluoromethyl; and

R_5 is a methyl.

9. A compound according to one of the claims 1 to 8, wherein said compound has an IC_{50} less than 10 μM in an *in vitro* inhibition of P I 3-K activity or an IC_{50} less than 20 μM in cellular inhibition of P I 3-K activity.

10. A pharmaceutical composition comprising the compound or a salt thereof according to one of the claims 1 to 8 and a pharmaceutically acceptable carrier.

11. A method of screening and characterizing the potency of a test compound as an inhibitor of phosphatidylinositol 3-kinase (PI 3-K) polypeptide, said method comprising the steps of (a) measuring activity of a PI 3-K polypeptide in the presence of a test compound according to one of the claims 1 to 8; (b) comparing the activity of the PI 3-K polypeptide in the presence of the test compound to the activity of the PI 3-K polypeptide in the presence of an equivalent amount of a known PI 3-K inhibitor as a reference compound, wherein lower activity of the PI 3-K polypeptide in the presence of the test compound than in the presence of the reference compound indicates that the test compound is a more potent inhibitor than the reference compound, and higher activity of the PI 3-K polypeptide in the presence of the test compound than in the presence of the reference compound indicates that the test compound is a less potent inhibitor than the reference compound.

12. A method to treat a disorder in which P I 3-K plays a role, comprising administering to a patient with said disorder an effective amount of the compound or a salt thereof according to one of the claims 1 to 8.

13. A method according to claim 12, wherein the disorder is a cancer or a disease of immunity and inflammation.

14. A method according to claim 12, wherein the disorder is disruption of PI 3-K function in leukocytes.

15. A method for inhibiting growth of cancer cells, comprising contacting said cancer cells with an effective amount of the compound or a salt thereof according to one of the claims 1 to 8.

16. The method according to claim 15, wherein said cancer cells are altered in PI 3-K mediated signaling via mutation in PTEN, amplification of the PIK3CA gene or mutations in PI 3-Kinase.

17. The method according to claim 15, wherein said cancers include breast, prostate, colon, lung, ovarian, and other cancers having altered PI 3-K activities.

18. A method for affecting PI 3-K mediated signaling in cells comprising contacting said cells with an effective amount of the compound or a salt thereof according to one of the claims 1 to 8.

19. The method according to claim 18, wherein said compounds affect PI 3-K mediated phosphorylation of Akt.